REMARKS

Reconsideration of this application, as amended, is respectfully requested.

Status of the claims

Claims 24, 28, 30-36, 40, 42-43 and 46-49 were pending in this application. All the above claims have been canceled without disclaimer prejudice to the filing of continuing applications. New claims 50-82 have been added. Support for the new claims can be found, for example, in the canceled claims and pages 8 and 9 of the specification as originally filed. Claims 50-82 are now pending in this application. No new matter has been added to the application as a result of the present amendment.

Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 24, 28, 30-36, 40, 42-43, and 46-49 stand rejected under 35 U.S.C. §112, first paragraph for lack of enablement. Applicants respectfully traverse the rejection. However, in order to expedite prosecution of the application, however, Applicants have canceled the rejected claims. Applicants respectfully submit that the rejection under § 112, first paragraph, of the aforementioned claims is now moot and that the § 112, first paragraph, rejection cannot be applied against the new claims.

The subject matter of new claims 50-82 is directed to compositions and methods that employ aromatase inhibitor exemestane in combination with at least one antineoplastic agent selected from the group consisting of epirubicin or docetaxel, in supperadditive antitumor effective amounts. The subject matter of the new claims is fully supported by the specification as acknowledged by the Examiner in the current office action (page 3, 4th full paragraph).

Rejection Under 35 U.S.C. § 112, second Paragraph

Claims 24, 28, 30-36, 40, 42-43, and 46-49 stand rejected under 35 U.S.C. 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regard as the invention. Applicants respectfully traverse this rejection. However, in order to expedite prosecution of this application, Applicants have canceled the rejected claims. Applicants submit that the rejection under § 112, second paragraph of the above cited claims is now moot.

Rejection Under 35 U.S.C. § 103

Claims 24, 28, 30-36, 40, 42-43, and 46-49 stand rejected under 35 U.S.C. §103 (a) as being unpatentable over the combination of Grem et al. (Am. J. Clin. Oncol., Vol. 11 (5), p. 528 1988)("Grem"), Tognella et al. (U.S. Patent No. 4,871,528)("Tognella") and Shashoua et al. (U.S. Patent No. 5,795,909) ("Shashoua"). The detailed basis for the Examiner's rejection can be found on pages 6-9. Applicants respectfully traverse the rejection. However, in order to expedite prosecution of this application, Applicants have canceled the rejected claims. Applicants submit that the rejection under § 103 of the above cited claims is now moot. The Applicants further submit that the rejection cannot be applied against the present claims.

The present invention, as claimed, is directed to methods and pharmaceutical compositions for treating breast cancer comprising the administration of at least one antineoplastic agent selected from the group consisting of epirubicin and docetaxel, and an aromatase inhibitor exemestane. The antineoplastic agents and aromatase are present in superadditive antitumor effective amounts. Applicants respectfully submit that the presently claimed invention is not obvious in view of the combination of Grem, Tognella and Shashoua.

Grem discloses a study designed to determine whether the combination of cyclophosphamide, doxorubicin and 5-fluoracil, together with an aromatase inhibitor, aminoglutethimide, can be safely administered with acceptable toxicity to a breast cancer patient. Grem concludes that the response rate of the combination composition is similar to the response rate of the antineoplastic agents alone. Therefore, Grem does not teach or suggest a combination therapy of antineoplastic agents and an aromatase inhibitor that has a superadditive antitumor effect.

Tognella relates to a synergistic effect of compositions containing an antitumor agent and reduced glutathione, which when administered alone, is completely devoid of any antitumor activity. See Tognella col. 4, lines 39-41. Thus, Tognella does not teach or suggest a synergistic antitumor effect of a combination therapy wherein each compound has known antitumor activity.

Shashoua relates to conjugates of pharmaceutical agents with highly lipophilic groups, which are said to have a different selectivity for various tissues than the unconjugated pharmaceutical agents. Shashoua, col. 3, lines 52-59. A myriad of categories of pharmaceutical agents are said to be conjugateable, including various antineoplastic agents and various aromatase inhibitors. Shashoua, col. 4, line 21 to col. 5, line 19, and col. 31. Shashoua does not disclose any compositions that include the combination of an antineoplastic agent and an aromatase inhibitor.

In fact, Tognella cautions the use of combination therapy with compounds where each compound has known antitumor activity as Tognella was concerned of the additive adverse side-effect. See Tognella col. 1, lines 42-45. Although Grem concludes that the combination of cyclophosphamide, doxorubicin and 5-fluoracil, together with aminoglutethimide could be tolerated in clinical trial, the combination composition did not result in synergistic response rate in comparison to the response rate of the antineoplastic agents administered alone.

Taken together, the combination of Grem, Togriella and Shashoua does not teach or suggest a superadditive antitumor effect of a combined use of the claimed antineoplastic agents and aromatase inhibitor, exemestane, for treating breast cancer. Exemestane and reduced glutathione are completely different compounds and differ by significant structural features. Based on Examiner's structure-function argument, (see for example, current office action pages 3-4) it would not have been obvious to one skilled artisan that a structurally different compound such as the aromatase inhibitor exemestane would be equivalent to reduced glutathione. Thus, in view of the prior art, it would not have been obvious to an ordinary skilled artisan the superadditive antitumor effect of a combined therapy of the claimed antineoplastic agents and aromatase inhibitor exemestane for the treatment of breast cancer.

Conclusion

In light of the present amendment and discussion above, the Applicant submit that new claims 50-82 are in allowable condition. Notice to this effect is respectfully requested.

Reconsideration of this application is respectfully requested and a favorable determination is earnestly solicited. Applicants urge the Examiner to contact the Applicants' undersigned representative at (312)913-0001 if the Examiner believes that this would expedite prosecution of this application.

Respectfully submitted,

Dated: Oct. 4, 2004

By: _____

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